Amendments to the Drawings

Please replace Figure 2 with the attached copy of the replacement Figure 2A-2B. This figure has been amended to label panels A and B.

Remarks

Prior to entry of this amendment, claims 1-48 were pending in the application. Claims 12-25, 31-39, 41-46 have been withdrawn from consideration. Claims 2-3 have been canceled. Applicants expressly reserve the right to pursue protection of any or all of the canceled subject matter in one or more continuing applications.

Claims 1, 7, 8-10, 24-25 and 40 have been amended.

Claim 1 is amended herein to be directed to specified polypeptides and to correct a typographical error. Applicants expressly reserve the right to prosecute any deleted subject matter in a continuation application. Claim 7 is amended herein to be in independent form. Claims 8-10 are amended herein to depend from claim 7. Support for the amendment of claims 24-25 can be found throughout the specification, such as on page 46, line 29 to page 49, line 4; page 50, line 6 to page 51, line 2; and page 52, lines 9-14. Claim 25 is also amended herein to correct a typographical error. Support for the amendment of claim 40 can be found throughout the specification, for example on page 30, lines 8-16; page 31, lines 7-23; and page 44, lines 1-4.

New claims 49-53 are added herein. Support for new claims 49-53 can be found in original claims 1 and 6-12, and throughout the specification, such as on page 34, line 8 to page 31, line 26.

No new matter is introduced by the foregoing amendments or the new claim. After entry of this amendment, **claims 1, 4-53 are pending in this application**. Consideration of the pending claims is requested.

Restriction Election (Point 1)

Applicants thank the Examiner for recombining Group I (claims 1-5, 26-30, and 39) with Group II (claims 6-11 and 40). Applicants also thank the Examiner for stating in the prior Office action that if product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all of the limitations of the allowable product claim will be rejoined in accordance with the provisions of M.P.E.P. § 821.04. In addition, process claims that depend from or otherwise include all of the limitations of the patentable product will be entered as a matter of right if presented prior to final rejection or allowance, whichever is earlier.

Drawings (Point 2)

Fig. 2 is objected to for failing to show the specific tissue expression of mRNA encoding NGEP, for the graphs appearing to be solid black, and for failing to distinguish between 2A and 2B. The graphs submitted with the original application do not appear black on the Applicant's copy, nor do they appear black in the original PCT application. A replacement figure is submitted herewith, which is identical to the original figure (and is printed out with high contrast). Replacement Fig. 2A-2B includes labels for panels A and B, rendering the rejection moot.

Objection to Claim 7 (Point 3)

The Office action acknowledges that claim 7 is free of the prior art. However, claim 7 is objected to for being dependent on a rejected base claim. Claim 7 is amended herein to be in independent form. Claims 8-11 depend from claim 7 or a dependent claim thereof. Thus, allowance of claims 7-11 is respectfully requested. If any minor amendments are required to place claims 7-11 in condition for allowance, the Examiner is requested to contact the undersigned for a telephone interview to expedite allowance.

Withdrawn process claims 24-25 are amended herein to depend from allowable claim 7 or a dependent claim thereof. The Office action dated July 28, 2006 confirmed that if a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all of the limitations of the allowable product claim will be rejoined in accordance with the provisions of M.P.E.P. § 821.04. In addition, process claims that depend from or otherwise include all of the limitations of the patentable product will be entered as a matter of right if presented prior to final rejection or allowance, whichever is earlier. Thus, Applicants respectfully request rejoinder and allowance of claims 24-25.

Rejection under 35 USC § 101(Point 4)

Claims 1-5, 39, 47 and 48 are rejected under 35 U.S.C. § 101 as allegedly there is no utility for the claimed polypeptides. Applicants respectfully disagree with this rejection.

MPEP § 2107.02 states:

> It is common and sensible for an applicant to identify several specific utilities for an invention, particularly where the invention is a product (e.g., a machine, an article of manufacture or a composition of matter). However, regardless of the category of invention that is claimed (e.g., product or process), an applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. 101 and 35 U.S.C. 112;

As noted in the Office action, the specification describes the use of the claimed polypeptides to (1) produce an antibody to detect prostate cells, (2) administer the polypeptide to a subject to generate an immune response, (3) administer NGEP to induce a cytotoxic T cell response. All of these utilities are specific, substantial and credible.

MPEP § 2107.02 further states:

> To properly reject a claimed invention under 35 U.S.C. 101, the Office must (A) make a *prima facie* showing that the claimed invention lacks utility, and (B) provide a sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing. *In re Gaubert*, 524 F.2d 1222, 1224, 187 USPQ 664, 666 (CCPA 1975) ("Accordingly, the PTO must do more than merely question operability - it must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability."). If the Office cannot develop a proper *prima facie* case and provide evidentiary support for a rejection under 35 U.S.C. 101, a rejection on this ground should not be imposed. See, e.g., *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

In the present application, the Office action provides no factual basis that would lead one skilled in the art to question the asserted utilities. Thus, Applicants submit that the utility rejection should be withdrawn. However, in the unlikely event that the utility rejection is maintained, submitted herewith is a copy of Das et al., Cancer Res. 67: 1-8, 2007. This amendment is submitted in accordance with MPEP § 2107.02, which sets forth that a rebuttal to an assertion of lack of utility can be submitted using a printed publication ("An applicant can do this using any combination of the following: amendments to the claims, arguments or reasoning, or new evidence submitted in an affidavit or declaration under 37 CFR 1.132, or in a printed publication"). Das et al. rebuts any *prima facie* case for a lack of utility. Specifically, Das et al. describe the production of antibodies to NGEP using methods described in the specification on page 31, line 28 to page 37, line 29. These antibodies were used to detect NGEP in protein extracts of prostate and prostate cancer. A band of 100 kDA (the predicted size) was detected in cells transfected with a nucleic acid encoding NGEP. In addition, a specific band at the expected

size was detected both in normal prostate and prostate cancers (see page 4 and Fig. 2 of Das et al.). Thus, the claimed polypeptides were demonstrated to have the "real world" utility of producing antibodies that detect prostate cells, such as for histological evaluation, as described in the specification.

Rejections under 35 USC § 112, First Paragraph (Points 5-8)

Claims 1-5, 26-30, 39 and 47-48 are rejected under 35 U.S.C. § 112, first paragraph as allegedly since these claims are not supported by a well established utility, one skilled in the art could not know *how to use* the claimed invention (emphasis from the Office action, Point 5). Applicants respectfully disagree with this rejection.

As discussed above, there is at least one specific, substantial and credible utility set forth in the specification. Moreover, in accordance with MPEP § 2107.02, submitted herewith is a printed publication (Das et al.) documenting the use of the claimed polypeptides to produce antibodies that specifically bind prostate cells and prostate cancer cells.

The specification discloses the production of polypeptides comprising SEQ ID NO: 1 (see page 21, line 21 to page 23, line 2). The specification further discloses domains of SEQ ID NO: 1 related to localization in the cell (see page 23, lines 13-30). The specification further describes specific fragments of SEQ ID NO: 1 that are at least 8 amino acids in length from a cytoplasmic region of SEQ ID NO: 1 that can be used to produce antibodies (see, for example, page 24, lines 8-20). The specification also discloses peptides of eight to ten amino acids in length that bind MHC (see, for example page 24, lines 22-26, line 2). Indeed, the amino acid sequence of eight 9-mers that bind MHC are presented in the specification on page 25, lines 15-24 (SEQ ID NOs: 3-10).

Indeed, the use of the claimed polypeptides to produce antibodies, and the use of the antibodies in Western blot analysis is described in the specification (see, for example, page 31, line 27 to page 39, line 4). In addition, Example 4 of the specification (see page 51, line 23 to page 52, line 7) describes the use of the claimed polypeptides to produce antibodies that can be utilized in Western blot analysis. The specification describes the use of antibodies that bind NGEP to detect prostate cells in a biological sample; exemplary ethods for detection of prostate cells (and/or prostate cancer cells) are described in the specification on page 46, line 29 to page 49, line 5.

Thus, there is more than adequate guidance provided in the specification for one of skill in the art to use the claimed polypeptides. This assertion is supported by the submission of Das et al., which describes the use of the claimed polypeptides to produce antibodies that specifically bind amino acids 875-933 of SEQ ID NO: 1, and the use of these antibodies to detect prostate cancer cells. Das et al. provides documentary evidence that one of skill in the art could readily make *and use* the claimed polypeptides given the guidance provided by the specification.

Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 6, 8-11 and 40 were rejected under 35 U.S.C. § 112, first paragraph as allegedly there is insufficient written description for polynucleotides encoding polypeptides at least 90% homologous to SEQ ID NO:1, or polypeptides that are 8-10 amino acids in length that bind MHC, or compositions including these polypeptides (Point 6). Claims 8-11 are amended herein to depend from claim 7, which was noted to be allowable, or a dependent claim thereof, rendering the rejection moot as applied to claims 8-11. Applicants respectfully disagree with this rejection as applied to claims 6 and 40, or any dependent claim thereof.

In order to expedite prosecution, the claims have been limited to polynucleotides encoding polypeptides encoding the amino acid sequence set forth as (a) SEQ ID NO: 1 or (b) 8-10 amino acids of SEQ ID NO: 1 that bind MHC. The cancellation of any subject matter should not be construed to validate the rejection; Applicants expressly reserve the right to prosecute the additional subject matter in a continuation application. This rejection will only be addressed with regard to the presently pending subject matter.

With regard to polynucleotides encoding the polypeptide sequence set forth as SEQ ID NO: 1 (claim 1, part a): The specification describes SEQ ID NO: 2, and exemplary nucleic acid sequence which encodes SEQ ID NO: 1. The specification further describes polynucleotide sequences that encode SEQ ID NO: 1, but differ due to the degeneracy of the genetic code (see the specification at page 27, line 1 to page 28, line 40). Applicants submit that this is sufficient written description for a polynucleotide encoding SEQ ID NO: 1.

Submitted as Exhibit A in support of this assertion is Example 11, part 1 (page 41-42) of the Revised Interim Written Description Guidelines Training Materials from the U.S. PTO

(hereinafter the "Guidelines"). This example is directed to the situation in which a full-length novel and un-obvious polypeptide (called "SEQ ID NO: 2") is disclosed. In this example, claim 1 is drawn to a genus of nucleic acids that encode the amino acid sequence set forth as SEQ ID NO: 2. The Guidelines state:

> "although only one species within the genus is disclosed, SEQ ID NO: 1 [an exemplary nucleotide sequence], a person of skill in the art could readily envision all the DNAs degenerate to SEQ ID NO: 1 by using a genetic code table. One of skill in the art would conclude that the applicant was in possession of the genus based on the specification and the general knowledge in the art concerning a genetic code table."

Thus, it is clear that in the present application, there is sufficient written description for polynucleotides encoding SEQ ID NO: 1, such as those that are degenerate due to the genetic code.

With regard to polynucleotides encoding eight to ten consecutive amino acids of SEQ ID NO: 1 (claim 1, part b): The specification describes several polypeptides of eight to ten consecutive amino acids of SEQ ID NO: 1 (see, for example, page 24, line 1 to page 25, line 14). Moreover, eight specific polypeptide sequences (SEQ ID NOs: 3-10) are provided that are nine consecutive amino acids in length of SEQ ID NO: 1. The HLA binding motif program (available for free use on the internet) confirms that these eight polypeptides will bind MHC (see the specification at page 25, lines 12-24).

Applicants submit that there is sufficient written description for a polynucleotide encoding a polypeptide comprising eight to ten consecutive amino acids of SEQ ID NO: 1.

Claims 6 and 8-11 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabled by the specification (Point 7). The Office action asserts that the specification is not enabling for (a) an amino acid sequence 90% homologous to SEQ ID NO: 1 or (2) at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO: 1, wherein the polypeptide is eight to ten amino acids in length and binds MHC. Applicants respectfully disagree with this rejection as may be applied to the claims as amended. Claims 10, 11 and 40 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification (Point 8). Claims 10 and 11 are amended herein to depend from claim 7, or a

dependent claim thereof, rendering the rejection moot as applied to these claims. Applicants respectfully disagree with the rejection as applied to claim 40. The rejections of claims 6 and 40 are addressed below.

The claims are currently drawn to polypeptides that are eight to ten consecutive amino acids of amino acids 157-933 of SEQ ID NO: 1 that bind MHC. The Office action alleges that one cannot extrapolate the disclosure of the specification to enable the claims as "the specification does not provide guidance or examples for making and using polypeptides" (see page 14).

1. The breadth of the claims

The claims are limited to polypeptides that are eight to ten consecutive amino acids of amino acids 157-933 of SEQ ID NO: 1 that bind MHC. Thus, the scope of the claims is limited to fragments of a specified length of a single amino acid sequence that can bind MHC class I. These fragments must include contiguous amino acids.

2. The nature of the invention

The invention is limited to polypeptides that consist of 8 to 10 consecutive amino acids of amino acids 157-933 of SEQ ID NO: 1 that bind MHC class I.

3. The state of the prior art

The prior art teaches how to identify immunogenic epitopes of a specified protein sequence that will bind MHC and induce an immune response. Computer programs were available at the time the application was filed wherein a technician can enter a specified amino acid sequence and the computer will predict which amino acid segment will bind MHC, such as HLA-A2.

To identify polypeptides consisting of eight to ten amino acids in length that bind MHC, the NGEP amino acid sequence can be entered into a computer program to identify epitopes of interest (see the specification, page 20, line 20 to page 21, line 12). Programs were publicly available for the identification of epitopes that bind MHC (see Parker et al., Scheme for ranking potential HLA-A2 binding peptides based on independent binding of individual peptide side-

chains, J Immunol. 152:163-75, 1994, provided on the internet at http://bimas.dcrt.nih.gov/molbio/hla_bind/ (print-out enclosed); see also Rammensee et al., Immunogenetics 50: 213-219, 1999). These methods for predicting MHC binding were well known to those of skill in the art at the time the provisional application was filed (see for example, Parker et al., *supra*). The production of nucleic acids encoding a specified amino acid sequence is well known in the art, and described in the specification (see for example, page 27, line 1 to page 31, line 26.

4. The level of skill of one of ordinary skill in the art

The level of skill of the average molecular biologist is high.

5. The level of predictability in the art

Computer programs can be used to predict which eight to ten consecutive amino acids of a specified polypeptide are likely to bind MHC. These programs rank polypeptides in order of predicted strength of the binding. Once the polypeptides are identified, a biological assay can be used to confirm that the eight to ten consecutive amino acids actually bind MHC. The generation of peptide specific cells is known in the art (see Tsang et al., J Natl Cancer Inst 87:982-90, 1995, copy enclosed). The production of nucleic acids encoding a specified polypeptide is routine, using materials such as expression vectors and host cells that are publicly available.

6. The amount of direction provided in the application

There is considerable direction provided in the application. The amino acid sequence of NGEP is provided as SEQ ID NO: 1 of the specification. Immunogenic peptides are clearly described in the specification. For example, immunogenic peptides, such as peptides that bind MHC are disclosed in the specification on page 23, line 3 to page 25, line 23. The specification also discloses that epitopes of use are 8-10 amino acids in length and have anchoring residues (see page 24, line 22 to page 25, line 12). Eight exemplary peptides are disclosed (see page 25, lines 16-23). Methods for the production of polynucleotides encoding these polypeptides are described in detail, for example on page 29, line 1 to page 31, line 26.

7. The existence of working examples

The specification describes eight 9-mers of SEQ ID NO: 1 that bind MHC (see page 25, lines 16-23).

In re Bundy, 642 F.2d 430, 434, 209 USPQ 48, 51-52 (CCPA 1981) held that appellant's disclosure was sufficient to enable one skilled in the art to use the claimed analogs of naturally occurring prostaglandins even though the specification lacked any examples of specific dosages, because the specification taught that the novel prostaglandins had certain pharmacological properties and possessed activity similar to known E-type prostaglandins. This is similar to the present application, wherein the specification teaches that the novel peptides have specific pharmacological properties and possess a specified activity (the binding of MHC). Moreover, specific physical properties of the claimed polypeptides are disclosed (the presence of anchor residues). The cloning and production of a fragment of NGEP is described in the specification (see page 51, line 15 to 28).

8. The quantity of experimentation needed to make or use the invention

Once a polypeptide consisting of eight to ten consecutive amino acids of SEQ ID NO: 1 is identified using am art-recognized program, polynucleotides encoding the polypeptide can readily be produced using standard methods in molecular biology. Thus, only very limited routine experimentation is required to produce the claimed polynucleotides.

Thus, given the very complete disclosure provided by the specification, only limited experimentation is required.

Claims Free of the Prior Art of Record (Point 9)

Applicants thank the Examiner for confirming that claims 1-11, 26-30, 39-40 and 47-48 are free of the prior art of record.

Request for Interview

If the present rejections are maintained, Applicants expressly request that the Examiner contact the undersigned prior to issuance of the next Office action, in order to arrange a telephonic interview to discuss any allowable subject matter. It is believed that a brief discussion

of the merits of the present application may expedite prosecution. This request is being submitted under MPEP §713.01, which indicates that an interview may be arranged in advance by a written request.

Conclusion

It is respectfully submitted that the present claims are in a condition for allowance. Should the Examiner have further questions or comments with respect to examination of this case, it is respectfully requested that the Examiner telephone the undersigned so that further examination of this application can be expedited.

Respectfully submitted,

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By _____
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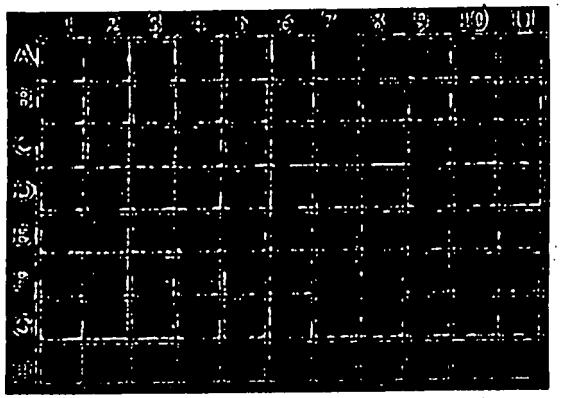
Registration No. 43,121

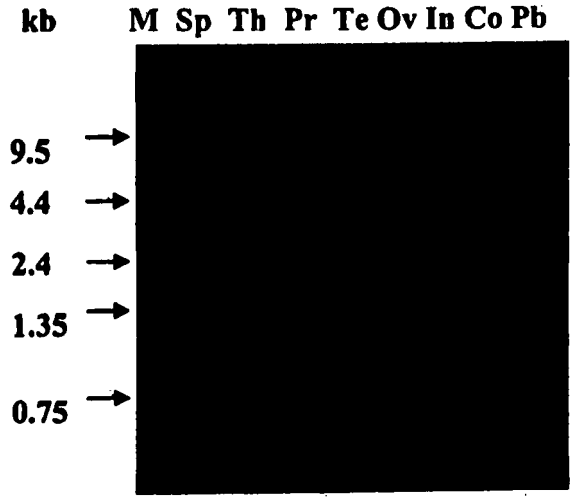
Amended to correct labeling and made more clear & visable

FIG. 2A



E8: Prostate

FIG. 2B



Pr: Prostate

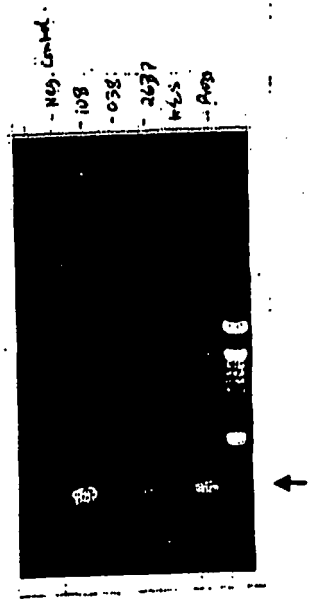


Fig. 2